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Among Hawaiian Women with Breast Cancer in Hawaii

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This is a cohort study of American women of Hawaiian ancestry who have one of the highest incidence rates of breast cancer in the world. It is designed to see if specific sources of dietary fat and alcohol use enhance breast cancer risk, and to determine if micronutrients and dietary fiber reduce risk.

The study has progressed well. It has recruited 7,790 Native Hawaiian women who returned a 26-page mail questionnaire. The surveillance of these women to identify incident cases of breast cancer is being done by the Hawaii Tumor Registry, which belongs to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program.

Thus far, 173 incident cases of breast cancer have been identified in this cohort. Preliminary results suggest the following: 1) early menopause may decrease breast cancer risk; 2) late childbirth may increase risk; 3) menopausal estrogens may increase risk; 4) alcohol intake may increase risk; 5) high dietary fat intake may increase risk; 6) high dietary fiber and beta-carotene consumption may decrease risk.

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Abraham Norcross 10/25/99  
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## INTRODUCTION

The subject of this study are Hawaiian American women who have one of the highest incidence rates of breast cancer in the world. They have a unique lifestyle and characteristically different dietary pattern which may contribute to their high risk for this disease. The purpose of the study is to identify those environmental and dietary factors that account for the development of breast cancer. Specifically, the study is designed to investigate the following: 1) the contribution of known risk factors, such as late age at first childbirth and late age at menopause, to the occurrence of breast cancer in Native Hawaiian women; 2) the association of other non-dietary exposures, such as exogenous estrogen use, with breast cancer risk; 3) the influence of dietary factors, such as dietary fat and alcohol use in enhancing, and of dietary fiber and micronutrients in reducing breast cancer; 4) the contribution of particular foods and food groups to the risk of breast cancer. The scope of the research consisted of five separate phases: 1) the development of a suitable 26-page mail questionnaire; 2) the recruitment of Native Hawaiian women who participated in the study; 3) the completion of data entry and data editing of the questionnaire; 4) surveillance of the study cohort to identify incident cases of breast cancer through the Hawaii Tumor Registry; 5) the preliminary data analysis.

## BODY

### Task 1. Recruitment of Study Cohort

Postcards were sent to 24,468 women believed to have Hawaiian ancestry. The 1,943 women who had moved out-of-state or for whom the postcards were undeliverable, were excluded. 22,525 (92.1%) remained in the study and were sent the questionnaire. After three mailings and additional effort, a total of 10,069 (44.7%) responded and returned the mailed questionnaire. Even though every effort was made to identify Hawaiian women based on Hawaiian surnames and use of the Voters' Registration list of Hawaiian women, 1546 respondents did not have Hawaiian ancestry, as reflected by their answers in the questionnaire. They were excluded from the study. The study cohort then consists of 8523 women with Native Hawaiian ancestry.

### Task 2. Completion of Data Entry

The questionnaires have been designed for automated data entry using high-speed optical scanners that are available at our institution. As a result, when the completed questionnaires were received from the study participants, they were scanned. We have completed the edit programs to check for internal inconsistency and to identify any discrepancies in the response recorded by study subjects. Each questionnaire has been systematically checked with the edit program by our research staff.

Thus far, 376 or 4.4% of 8,523 women had unusable questionnaires. Among the 8,147 remaining women, 357 already had a diagnosis of breast cancer, so they were also excluded. Consequently, 7,790 Hawaiian women remained in the study.

### Task 3. Surveillance of the Cohort

We have been following this cohort to determine cancer occurrence and mortality. We are well equipped for surveillance of cancer since the Hawaii Tumor Registry is a statewide, population-based registry and is included in the NCI's SEER Program. In addition, the Registry is part of the Cancer Research Center of Hawaii. The registry reports all new cases of cancer, and follows patients for survival information. We will continue to follow the cohort for cancer occurrence by computer linkage to the tumor registry to identify newly-diagnosed cancer cases. To identify deaths occurring in the study areas and elsewhere in the U.S., we will use the state death files of Hawaii and the National Death Index.

After the third year of the study, we had identified 56 incident cases of breast cancer. By the end of the fourth year, 122 incident cases were recorded. Now, we have identified 173 incident cases.

### Task 4. Surveillance and Preliminary Data Analysis

Preliminary data are available on the association of various exposures with breast cancer. All of the data in these tables have been adjusted for age. Table 1 suggests that among the 5,110 women who had undergone menopause, the risk of breast cancer was lower (0.7) for those who had menopause before the age of 45.

Table 1  
Age at Menopause and Breast Cancer

Age at Menopause	No. of Cases	No. of Women	Relative Risk	95% Confidence Interval
45+ years	86	3126	1.0	--
<45 years	35	1984	0.7	0.5-1.0

Table 2 presents the association of age at first birth with breast cancer risk. Women who gave birth at age 26 or later or who did not have children, had a greater risk than women who gave birth before the age of 21.

Table 2  
Age at First Birth and Breast Cancer

Age at First Birth	No. of Cases	No. of Women	Relative Risk	95% Confidence Interval
<21 years	64	3292	1.0	--
21-25 years	60	2667	1.1	0.8-1.6
26+ years	23	884	1.4	0.9-2.3
Nulliparous	26	926	1.5	0.9-2.4

The relation of menopausal estrogen use to breast cancer is shown in Table 3. Thirty-eight per cent of the women had taken menopausal estrogens and their risk of breast cancer was slightly higher than that of non-users.

Table 3  
Menopausal Estrogens and Breast Cancer

Estrogen	No. of	No. of	Relative	95% Confidence
User	Cases	Women	Risk	Interval
No	96	4663	1.0	--
Yes	68	2853	1.1	(0.8-1.5)

Table 4 presents the association of alcohol intake with breast cancer in Hawaiian women. Alcohol drinkers had a higher risk of breast cancer than non-drinkers.

Table 4  
Alcohol Intake and Breast Cancer

Alcohol	No. of	No. of	Relative	95% Confidence
Intake	Cases	Women	Risk	Interval
Non-Drinker	140	6313	1.0	
Drinker	30	1096	1.3	0.9-1.9

In Table 5, the women are separated into tertile groupings, based on their consumption of dietary fat, as recorded in the questionnaire. Thus far, it shows that there is no clear association between the intake of dietary fat and breast cancer.

Table 5  
Dietary Fat and Breast Cancer

Tertile (g/day)	No. of Cases	No. of Women	Relative Risk	95% Confidence Interval
1 <54	54	2595	1.0	--
2 54-90	60	2591	1.1	0.8-1.6
3 >90	59	2583	1.1	0.8-1.6

In Tables 6 and 7, there is a suggestion that a high intake of dietary beta-carotene and dietary fiber reduces the risk of breast cancer.

Table 6  
Dietary Beta-Carotene and Breast Cancer

Tertile (mcg/day)	No. of Cases	No. of Women	Relative Risk	95% Confidence Interval
1 <3297	59	2595	1.0	--
2 3297-6686	54	2591	0.9	0.6-1.3
3 >6686	60	2583	0.9	0.6-1.3

Table 7  
Dietary Fiber and Breast Cancer

Tertile (g/day)	No. of Cases	No. of Women	Relative Risk	95% Confidence Interval
1 <17	61	2595	1.0	--
2 17-30	55	2591	0.6	0.6-1.2
3 >30	57	2583	0.6	0.6-1.1

### Discussion

This is an efficient study because it uses data collection instruments that have been developed, tested and validated. In addition, it is unique in proposing to investigate one of the world's populations at highest risk for breast cancer -- Native Hawaiian women.

The recruitment of study subjects has been completed. We were successful in eliciting the cooperation of 7,790 Native Hawaiian women who returned the mail questionnaire. We expect a negligible rate of loss to follow-up due to out-migration. In a study in which a random sample of 2000 residents were followed in Hawaii, there was less than a 7% loss after 5 years of follow-up. For the Native Hawaiian population, this number is expected to be much lower because relatively few Hawaiians migrate elsewhere.

The preliminary results suggest that early menopause may decrease breast cancer risk and that late age at childbirth may increase risk. These data are consistent with past reports on the risk factors associated with breast cancer (1). The use of menopausal estrogens may also increase risk, as suggested by some investigators (2,3). However, other researchers have not been able to confirm this suspected association (4-6). Our data are equivocal on the association of dietary fat

with breast cancer, as supported by past reports (7-11). There may be an inverse association in the intake of micronutrients and dietary fiber with breast cancer risk, as found in past studies (12,13), but more work needs to be done to substantiate this preliminary finding in our study.

## KEY RESEARCH ACCOMPLISHMENTS

- Early menopause may decrease breast cancer risk: among women who have had menopause, since those with menopause <45 years of age had a Relative Risk of 0.7 (95% Confidence Interval, 0.5-1.0) compared with women whose menopause occurred at age 45 or older.
- Nulliparity or childbirth after age 25 may increase risk: women who did not give birth had a RR of 1.5 (95% CI, 0.9-2.4) compared with women who gave birth before the age of 21. For women who gave birth at age 25 or older, the RR was 1.4 (95% CI, 0.9-2.3).
- Menopausal estrogen users may or may not have an increased breast cancer risk: estrogen users had a RR of 1.1 (95% CI, 0.8-1.5) compared with nonusers.
- Alcohol drinkers may have an increased risk: alcohol drinkers had a RR of 1.3 (95% CI, 0.9-1.9) compared with nondrinkers.
- High dietary fat consumers may or may not have an increased risk of breast cancer: high consumers had a RR of 1.1 (95% CI, 0.8-1.6) compared with low consumers of dietary fat.
- High beta-carotene consumers may or may not have a decreased risk: women consuming large amounts of beta-carotene had a RR of 0.9 (95% CI, 0.6-1.3) compared with low consumers of beta-carotene.
- High consumers of dietary fiber may have a decreased risk: women consuming large amounts of dietary fiber had a RR of 0.6 (95% CI, 0.6-1.1) compared with low consumers of dietary fiber.

## REPORTABLE OUTCOMES

Presentations- Poster Session at DoD Breast Cancer Research Program: An Era of Hope, in Washington, D.C. from October 31-November 4, 1997.

Manuscripts- Pending

Patents- Not applicable

Degrees Obtained- Not applicable

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Funding applied- None

Employment opportunities- None

## CONCLUSIONS

We have recruited 8,523 Hawaiian women into the study. Of these, 7,790 have usable questionnaires and were not prevalent cases who had already been diagnosed with breast cancer. As a result, we will be able to conduct a long-term prospective study of breast cancer in this high risk population. Thus far, 173 incident cases of breast cancer have been identified.

Preliminary results, after statistical adjustment for age, show the following:

1. Early menopause may decrease breast cancer risk;
2. Late childbirth, especially after age 25, may increase risk;
3. Menopausal estrogen users may have an increased risk;
4. Alcohol drinkers may have an increased risk;
5. High dietary fat consumers may have an increased risk;
6. High beta-carotene consumers may have a decreased risk;
7. High dietary fiber consumers may have a decreased breast cancer risk.

Surveillance will continue in this cohort of Native Hawaiian women so that detailed analyses can be done with more incident cases to characterize the factors that places these women at a high risk for breast cancer. In the meantime, the preliminary results of the study are consistent with what is known about the suspected protective and harmful factors associated with breast cancer.

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## FINAL REPORT

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Meeting- Poster Session at DoD Breast Cancer Research Program: An Era of Hope, in Washington, D.C. from October 31-November 4, 1997.

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